

Art Unit : Unknown
Examiner : Unknown

Commissioner for Patents
Washington, D.C. 20231

Prior to examination, please amend the application as follows:

Please insert the following paragraph after the title on page 1 of the application:

This application is a divisional of and claims priority under 35 U.S.C. §120 to U.S. Application No. 09/398,395, filed September 17, 1999, which claims benefit under 35 USC §119(e) of U.S. Provisional Application No. 60/150,262, filed August 23, 1999, U.S. Provisional Application No. 60/130,628, filed April 22, 1999, and U.S. Provisional Application No. 60/100,993, filed September 18, 1998.--

Please replace the Sequence Listing filed with the application with the enclosed Sequence Listing.

Please cancel claims 1-106 and 108-162 without prejudice to continued prosecution.

Vince Defante
Typed or Printed Name of Person Signing Certificate

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The pending claims, including new claims 163-242, are as follows.

107. An isolated synthase having a region with 40% or greater sequence identity to residues 579 to 847 of SEQ ID NO: 44, wherein one or more amino acid residues of said synthase that align with amino acids at positions 584, 587, 606, 609, 610, 688, 713, 714, 715, 716, 719, 753, 757, 831, 834, 835, 839, 841 and 842 of SEQ ID NO: 44 are residues other than the following ordered arrangements of residues:

163-242

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Ordered Arrangement of Residues															
	584	587	606	609	610	688	713	714	715	716	719	753	757	831	834
	835	839	841	842											
A	C	W	I	I	S	Y	T	T	T	Y	L	C	D	V	T
B	C	W	I	I	S	Y	T	S	T	Y	L	C	D	I	T
C	G	W	I	A	S	Y	T	C	G	Y	L	C	D	M	L
D	G	W	I	A	S	Y	T	S	G	Y	L	C	D	M	L
E	G	W	L	T	S	Y	S	A	G	Y	L	A	N	A	L
F	G	W	L	T	S	Y	S	T	V	H	L	G	D	A	V
G	C	W	L	T	S	Y	S	A	G	Y	L	A	N	A	L
H	L	W	I	V	T	Y	S	V	G	N	L	F	D	V	L
I	P	W	I	V	T	Y	S	T	A	G	L	S	D	A	L
J	A	W	V	C	G	F	T	S	C	I	M	G	N	C	S
K	N	F	V	L	T	Y	E	I	T	A	T	G	N	I	T
L	C	W	N	I	T	Y	S	I	S	Y	L	L	G	V	M
M	S	W	V	L	T	Y	S	T	S	A	L	L	G	L	S
N	N	F	F	L	V	N	A	S	L	A	L	L	N	A	M
O	C	W	N	I	T	Y	I	S	G	P	L	L	D	A	I
P	C	W	N	V	T	Y	I	G	G	I	L	L	D	A	I
Q	C	Y	L	L	T	F	A	V	T	M	T	G	N	I	T
R	C	W	I	I	T	Y	S	I	S	A	I	L	N	V	I
S	S	W	F	I	V	Y	S	S	A	V	I	L	N	V	I
T	S	W	I	A	T	Y	S	V	S	S	I	L	D	A	I
U	N	W	N	L	T	Y	S	I	S	S	I	F	N	S	M
V	F	L	A	Q	T	Y	S	I	G	Q	L	S	D	T	I
W	I	S	S	T	V	Y	S	I	A	L	V	G	N	M	F
X	Y	L	C	I	T	Y	S	C	G	H	S	L	G	F	G
Y	G	S	F	I	T	Y	S	S	S	V	I	L	N	A	V
Z	Y	W	A	C	T	Y	S	S	G	M	L	L	D	L	I
AA	A	A	N	L	T	N	A	L	T	S	T	C	M	L	L
BB	F	L	C	V	T	Y	S	S	A	Y	V	L	G	L	L
CC	F	W	A	M	T	Y	N	T	G	M	L	S	D	I	M
DD	Y	M	C	V	T	F	V	S	S	L	I	L	G	F	V
EE	V	S	G	Q	V	M	S	A	L	G	V	W	N	V	F
FF	C	S	G	T	T	M	F	F	A	L	V	G	N	L	F
GG	C	S	G	T	T	M	S	F	A	L	I	G	N	L	F
HH	C	A	G	T	T	M	S	F	A	L	I	G	N	L	F
II	I	W	V	I	S	Y	T	T	G	L	V	I	D	L	S
JJ	Y	W	A	C	T	Y	S	S	G	M	L	G	D	V	I
KK	C	W	I	I	S	Y	T	T	T	Y	L	C	D	I	T
LL	C	W	I	I	S	Y	T	T	T	Y	L	C	D	I	T
MM	C	W	N	I	T	Y	S	I	S	G	M	L	D	A	M
NN	F	A	A	Q	T	Y	S	I	G	Q	L	S	D	T	I
OO	F	A	I	A	T	Y	S	V	A	S	I	L	D	A	I

[illegible]

163. The synthase of claim 107, wherein said synthase has 50% or greater sequence identity to residues 579 to 847 of SEQ ID 44.
164. The synthase of claim 107, wherein said synthase has 60% or greater sequence identity to residues 579 to 847 of SEQ ID 44.
165. The synthase of claim 107, wherein said synthase catalyses the formation of a terpenoid product from a monoterpene substrate.
166. The synthase of claim 107, wherein said synthase catalyses the formation of a terpenoid product from a sesquiterpene substrate.
167. The synthase of claim 107, wherein said synthase catalyses the formation of a terpenoid product from a diterpene substrate.
168. The synthase of claim 165, wherein said product is a cyclic terpenoid hydrocarbon.
169. The synthase of claim 166, wherein said product is a cyclic terpenoid hydrocarbon.
170. The synthase of claim 167, wherein said product is a cyclic terpenoid hydrocarbon.
171. The synthase of claim 165, wherein said product is an acyclic terpenoid hydrocarbon.
172. The synthase of claim 166, wherein said product is an acyclic terpenoid hydrocarbon.
173. The synthase of claim 167, wherein said product is an acyclic terpenoid hydrocarbon.
174. The synthase of claim 165, wherein said product is a cyclic hydroxylated terpenoid hydrocarbon.
175. The synthase of claim 166, wherein said product is a cyclic hydroxylated terpenoid hydrocarbon.
176. The synthase of claim 167, wherein said product is a cyclic hydroxylated terpenoid hydrocarbon.

191. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Met, Ile, Val and Leu.

192. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Arg and Lys.

193. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Gln, Asn and His.

194. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Cys, Ser and Thr.

195. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Phe, Tyr and Trp.

196. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Pro, Gly, and Ala.

197. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Glu and Asp.

198. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Met, Ile, Val and Leu.

199. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Arg and Lys.

200. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Gln, Asn and His.

201. The synthase of claim 107, wherein said amino acid at position 715 is selected from the group consisting of Cys, Ser and Thr.

202. The synthase of claim 107, wherein said amino acid at position 715 is selected from the group consisting of Phe, Tyr and Trp.

203. The synthase of claim 107, wherein said amino acid at position 715 is selected from the group consisting of Pro, Gly, and Ala.

204. The synthase of claim 107, wherein said amino acid at position 715 is selected from the group consisting of Glu and Asp.

205. The synthase of claim 107, wherein said amino acid at position 715 is selected from the group consisting of Met, Ile, Val and Leu.

206. The synthase of claim 107, wherein said amino acid at position 715 is selected from the group consisting of Arg and Lys.

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207. The synthase of claim 107, wherein said amino acid at position 715 is selected from the group consisting of Gln, Asn and His.

208. The synthase of claim 107, wherein said amino acid at position 716 is selected from the group consisting of Cys, Ser and Thr.

209. The synthase of claim 107, wherein said amino acid at position 716 is selected from the group consisting of Phe, Tyr and Trp.

210. The synthase of claim 107, wherein said amino acid at position 716 is selected from the group consisting of Pro, Gly, and Ala.

211. The synthase of claim 107, wherein said amino acid at position 716 is selected from the group consisting of Glu and Asp.

212. The synthase of claim 107, wherein said amino acid at position 716 is selected from the group consisting of Met, Ile, Val and Leu.

213. The synthase of claim 107, wherein said amino acid at position 716 is selected from the group consisting of Arg and Lys.

214. The synthase of claim 107, wherein said amino acid at position 716 is selected from the group consisting of Gln, Asn and His.

215. The synthase of claim 107, wherein said amino acid at position 719 is selected from the group consisting of Cys, Ser and Thr.

216. The synthase of claim 107, wherein said amino acid at position 719 is selected from the group consisting of Phe, Tyr and Trp.

217. The synthase of claim 107, wherein said amino acid at position 719 is selected from the group consisting of Pro, Gly, and Ala.

218. The synthase of claim 107, wherein said amino acid at position 719 is selected from the group consisting of Glu and Asp.

219. The synthase of claim 107, wherein said amino acid at position 719 is selected from the group consisting of Met, Ile, Val and Leu.

220. The synthase of claim 107, wherein said amino acid at position 719 is selected from the group consisting of Arg and Lys.

221. The synthase of claim 107, wherein said amino acid at position 719 is selected from the group consisting of Gln, Asn and His.

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308	2309	2310	2311	2312	2313	2314	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354	2355	2356	2357	2358	2359	2360	2361	2362	2363	2364	2365	2366	2367	2368	2369	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398	2399	2400	2401	2402	2403	2404	2405	2406	2407	2408	2409	2410	2411	2412	2413	2414	2415	2416	2417	2418	2419	2420	2421	2422	2423	2424	2425	2426	2427	2428	2429	2430	2431	2432	2
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222. The synthase of claim 107, wherein said amino acid at position 753 is selected from the group consisting of Cys, Ser and Thr.

223. The synthase of claim 107, wherein said amino acid at position 753 is selected from the group consisting of Phe, Tyr and Trp.

224. The synthase of claim 107, wherein said amino acid at position 753 is selected from the group consisting of Pro, Gly, and Ala.

225. The synthase of claim 107, wherein said amino acid at position 753 is selected from the group consisting of Glu and Asp.

226. The synthase of claim 107, wherein said amino acid at position 753 is selected from the group consisting of Met, Ile, Val and Leu.

227. The synthase of claim 107, wherein said amino acid at position 753 is selected from the group consisting of Arg and Lys.

228. The synthase of claim 107, wherein said amino acid at position 753 is selected from the group consisting of Gln, Asn and His.

229. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Cys, Ser and Thr.

230. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Phe, Tyr and Trp.

231. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Pro, Gly, and Ala.

232. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Glu and Asp.

233. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Met, Ile, Val and Leu.

234. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Arg and Lys.

235. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Gln, Asn and His.

236. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Cys, Ser and Thr.

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237. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Phe, Tyr and Trp.

238. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Pro, Gly, and Ala.

239. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Glu and Asp.

240. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Met, Ile, Val and Leu.

241. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Arg and Lys.

242. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Gln, Asn and His.

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REMARKS

Applicants respectfully request entry of the amendments and remarks submitted herein. Claims 1-106 and 108-162 have been canceled. New claims 163-242 have been added. Support for new claims 163-242 can be found in the originally filed claims and throughout the specification. Accordingly, claims 107 and 163-242 are currently pending. Attached is a marked-up version of the changes being made by the current amendments. Applicants note that claim 107 correspond to Group 11 in the May 4, 2001 Restriction Requirement issued by the Examiner in the parent case. Consideration of the pending application is respectfully requested.

The Sequence Listing

Applicants submit herewith a paper copy of the Sequence Listing and a request to transfer the computer readable form of the Sequence Listing from the parent application to the present application. The Sequence Listing submitted herewith to replace the originally-filed Sequence Listing serves to conform SEQ ID NO:1 and SEQ ID NO:2 to the sequences of GenBank Accession Number Q40577 referred to on page 14 of the specification. The tobacco epiaristolochene synthase (TEAS) nucleic acid and protein sequences in SEQ ID NO:1 and 2 of the original Sequence Listing are those of Accession No. L04680. L04680 differs from the sequence of Q40577 at 22 nucleotides, resulting in differences at 6 amino acid positions (residues 44, 55, 62, 73, 89 and 388). The annotation for GenBank Accession No. Q40577 notes the differences between Q40577 and L04680. The text of the Q40577 GenBank annotations is enclosed. The differences between the two TEAS sequences do not correspond to any of the nineteen residues of TEAS referred to throughout the specification (*i.e.*, residues 270, 273, 294, 297, 298, 376, 401, 402, 403, 404, 407, 440, 444, 516, 519, 520, 525, 527, and 528). Accordingly, the sequence amendments to the Sequence Listing submitted herewith do not constitute new matter.

The Sequence Listing submitted herewith also clarifies or corrects several identifier fields within the originally-filed Sequence Listing. For example, SEQ ID NOS:1-12 originally used the mutant designation in the identifier field for organism. SEQ ID NOS:1-12 now identify *Nicotiana tabacum* as the organism. By way of this amendment, Applicants have also included the description for the 'n' nucleotides in SEQ ID NO:11 and the 'Xaa' residues in SEQ ID NO:12 that were absent in the originally-filed Sequence Listing. Applicants have also removed

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the stop codon from the polypeptide sequences of the Sequence Listing, as required under 37 CFR §1.821-1.825. The herein-described corrections to the Sequence Listing do not constitute an introduction of new matter.

CONCLUSION

Applicant asks that claim 107 and 163-242 be examined. The filing fee enclosed herewith reflects the claim amendments herein. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: June 28, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

A paragraph concerning related applications was inserted on page 1 of the application after the title.

The Sequence Listing filed with the application was replaced with the Sequence Listing enclosed herein.

In the Claims:

Claims 1-106 and 108-162 have been cancelled.

The following new claims were added:

163. The synthase of claim 107, wherein said synthase has 50% or greater sequence identity to residues 579 to 847 of SEQ ID 44.

164. The synthase of claim 107, wherein said synthase has 60% or greater sequence identity to residues 579 to 847 of SEQ ID 44.

165. The synthase of claim 107, wherein said synthase catalyses the formation of a terpenoid product from a monoterpene substrate.

166. The synthase of claim 107, wherein said synthase catalyses the formation of a terpenoid product from a sesquiterpene substrate.

167. The synthase of claim 107, wherein said synthase catalyses the formation of a terpenoid product from a diterpene substrate.

168. The synthase of claim 165, wherein said product is a cyclic terpenoid hydrocarbon.

169. The synthase of claim 166, wherein said product is a cyclic terpenoid hydrocarbon.

170. The synthase of claim 167, wherein said product is a cyclic terpenoid hydrocarbon.

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171. The synthase of claim 165, wherein said product is an acyclic terpenoid hydrocarbon.

172. The synthase of claim 166, wherein said product is an acyclic terpenoid hydrocarbon.

173. The synthase of claim 167, wherein said product is an acyclic terpenoid hydrocarbon.

174. The synthase of claim 165, wherein said product is a cyclic hydroxylated terpenoid hydrocarbon.

175. The synthase of claim 166, wherein said product is a cyclic hydroxylated terpenoid hydrocarbon.

176. The synthase of claim 167, wherein said product is a cyclic hydroxylated terpenoid hydrocarbon.

177. The synthase of claim 165, wherein said product is an acyclic hydroxylated terpenoid hydrocarbon.

178. The synthase of claim 166, wherein said product is an acyclic hydroxylated terpenoid hydrocarbon.

179. The synthase of claim 167 wherein said product is an acyclic hydroxylated terpenoid hydrocarbon.

180. The synthase of claim 107, wherein said amino acid at position 587 is selected from the group consisting of Cys, Ser, and Thr.

181. The synthase of claim 107, wherein said amino acid at position 587 is selected from the group consisting of Phe, Tyr and Trp.

182. The synthase of claim 107, wherein said amino acid at position 587 is selected from the group consisting of Pro, Gly, and Ala.

183. The synthase of claim 107, wherein said amino acid at position 587 is selected from the group consisting of Glu and Asp.

184. The synthase of claim 107, wherein said amino acid at position 587 is selected from the group consisting of Met, Ile, Val and Leu.

185. The synthase of claim 107, wherein said amino acid at position 587 is selected from the group consisting of Arg and Lys.

186. The synthase of claim 107, wherein said amino acid at position 587 is selected from the group consisting of Gln, Asn and His.

187. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Cys, Ser and Thr.

188. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Phe, Tyr and Trp.

189. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Pro, Gly, and Ala.

190. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Glu and Asp.

191. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Met, Ile, Val and Leu.

192. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Arg and Lys.

193. The synthase of claim 107, wherein said amino acid at position 606 is selected from the group consisting of Gln, Asn and His.

194. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Cys, Ser and Thr.

195. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Phe, Tyr and Trp.

196. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Pro, Gly, and Ala.

197. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Glu and Asp.

198. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Met, Ile, Val and Leu.

199. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Arg and Lys.

200. The synthase of claim 107, wherein said amino acid at position 714 is selected from the group consisting of Gln, Asn and His.

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215. The synthase of claim 107, wherein said amino acid at position 719 is selected from the group consisting of Cys, Ser and Thr.

230. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Phe, Tyr and Trp.

231. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Pro, Gly, and Ala.

232. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Glu and Asp.

233. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Met, Ile, Val and Leu.

234. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Arg and Lys.

235. The synthase of claim 107, wherein said amino acid at position 834 is selected from the group consisting of Gln, Asn and His.

236. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Cys, Ser and Thr.

237. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Phe, Tyr and Trp.

238. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Pro, Gly, and Ala.

239. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Glu and Asp.

240. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Met, Ile, Val and Leu.

241. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Arg and Lys.

242. The synthase of claim 107, wherein said amino acid at position 835 is selected from the group consisting of Gln, Asn and His.

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